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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/652,676	08/28/2003	Joseph Utermohlen	191/001/DIV1	2546

23874 7590 02/08/2008

VENTANA MEDICAL SYSTEMS, INC.
ATTENTION: LEGAL DEPARTMENT
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TUCSON, AZ 85755

EXAMINER	
TUNG, JOYCE	
ART UNIT	**PAPER NUMBER**
1637	

MAIL DATE	DELIVERY MODE
02/08/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/652,676	UTERMOHLEN ET AL.	
	Examiner	Art Unit	
	Joyce Tung	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-14 and 18-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-14 and 18-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/1/07 has been entered.

The response filed 10/30/07 to the Office action has been entered. Claims 9-14, and 18-20.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 9-14 and 19-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schwartz (4,886,741, issued December 12, 1989).

Schwartz et al. disclose using volume exclusion agents to enhance in situ hybridization rates between short oligonucleotide probe and their target polynucleotides where the cells containing the target polynucleotide are adhered onto a glass substrate (See the Abstract, column 2, lines 30-35). The volume exclusion agent is at a concentration of 2% to 25% (w/v) of the reaction mixture (column 2, lines 48-53). One of the volume exclusion agents is dextran sulfate (See column 3, lines 1-3, column 6, lines 31-33, and column 10, lines 25-26). The preferred polymer weight is at least 10,000 daltons (See column 3, lines 14-15). The tissues are prepared by freezing, perfusion and embedding with paraffin prior to sectioning (See column 3, lines 67-68). The probe is labeled with fluorophores (See column 5, lines 24-25).

Schwartz et al. do not disclose that an automated staining system having evaporation inhibitor liquid covering a polynucleotide hybridization buffer-covered target on the slide is used.

However, an automatic or mechanical means to replace a manual activity which accomplished the same result is not sufficient to distinguish over the prior art (See MPEP, 2144.04, III) The statement is cited as follows:

> In re Venner, 262 F.2d 91, 95, 120 USPQ 193, 194 (CCPA 1958) (Appellant argued that claims to a permanent mold casting apparatus for molding trunk pistons were allowable over the prior art because the claimed invention combined "old permanent-mold structures together with a timer and solenoid which automatically actuates the

known pressure valve system to release the inner core after a predetermined time has elapsed." The court held that broadly providing an automatic or mechanical means to replace a manual activity which accomplished the same result is not sufficient to distinguish over the prior art.).

Schwartz does not disclose the exact molecular weight of dextran sulfate.

It would further have been prima facie obvious to perform routine optimization using reagents, as noted in *In re Aller*, 105 USPQ 233 at 235,

> More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Routine optimization is not considered inventive and no evidence has been presented that the selection specific molecular weight of dextran sulfate was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

The response argues that Schwartz et al. do not disclose a low molecular weight dextran sulfate for use as an exclusion agent in polynucleotide hybridization and in fact Schwartz et al. disclose that the molecular weight of dextran sulfate which is 500,000 daltons is used at a concentration of about 5-10% (w/v) and three different polymers are useful as volume exclusion agents including polyethylene glycol, anionic polymer of polyacrylate or polymethylacrylate and generic dextran sulfate. However, Schwartz et al. disclose that the preferred polymer weight is at least 10,000 daltons and no more than 2,000,000 daltons (See column 3, lines 14-15). The molecular weight as disclosed by Schwartz satisfies the limitation that low molecular weight

dextran sulfate has a molecular weight range from about 8,000 to about 16,000 daltons. The teachings of Schwartz do not exclude the preferred polymer which is dextran sulfate.

The response further argues that Schwartz et al. disclose a manual procedure and do not disclose "automated in situ hybridization", the specification indicates that Applicants discovered that high viscosity inhibits hybridization in Ventana's automated environment and then found the solution-a low-viscosity buffer which is necessary for optimal hybridization and the instant claims represent an improvement from that perspective. However, although the instant claims may be an improved method, such an improvement is not necessary unobvious. Based upon the teachings of Schwartz et al. as set forth above, one of ordinary skill in the art would have been motivated to use dextran sulfate with a molecular weight that is at least 10,000 daltons with a reasonable expectation of success.

The response argues that reliance on *Venner* is misplaced because Applicants' claimed invention does not replace a manual activity with an automated one, Applicants are claiming an improved method *of in situ* hybridization in an automated tissue staining environment by automatically hybridizing a target with a polynucleotide probe composition in the presence of low molecular weight dextran sulfate having a molecular weight range from about 8,000 to about 16,000 daltons. However, as noted above, an improvement over the prior art is not necessary patentable – it must also be unobvious. Based upon the teachings of Schwartz et al. as set forth above, one of ordinary skill in the art would have been motivated to use dextran sulfate with a molecular weight that is at least 10,000 daltons with a reasonable expectation of success.

The response also argues that reliance on *Aller* is misplaced because if Applicants had routinely optimized, they would have changed the concentration of the exclusion agent, as

varying the molecular weight was not taught in the prior art of ISU. However, Schwartz et al. disclose that the preferred polymer weight is at least 10,000 daltons (See column 3, lines 14-15). One of ordinary skill in the art would have been motivated to optimize a hybridization condition with various molecular weight of dextran sulfate.

Thus based upon the analysis above, the rejection is maintained.

4. Claim 18 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Schwartz (4,886,741, issued December 12, 1989) as applied to claims 9-14 and 19-21 above, and further in view of Towne et al. (6,855,552, issued February 15, 2005).

The teachings of Schwartz are set forth in section 3 above. Schwartz does not disclose that the probe composition is arrayed on a solid substrate.

Towne et al. disclose automated immunohistochemical and in situ hybridization assay (See the Abstract and column 4, lines 49-63). The method of Towne et al. comprises automatic hybridization, removal and detection steps (see entire document). Towne et al. also disclose that biological sample includes tissue arrays (See column 14, lines 8-14). This teaching suggests that after hybridization on a target, the probe composition is arrayed on a solid substrate.

One of ordinary skill in the art would have been motivated to apply the tissue array of Towne et al. to the method of Schwartz because it increases the accessibility of various molecules to their respective targets and to improve tissue and cell readability of biological sample on automated instruments (See column 1, lines 26-32). It would have been prima facie obvious to apply the probe composition, which is arrayed on a solid substrate.

The response argues that Towne et al. US 6,855,552, issued Feb. 15, 2005 is not qualified as prior art. However, Towne et al. US 6,855,552 is a continuation of application No. 09/259,240, filed on Feb. 26, 1999, now pat. No. 6,296,809. The patent No. 6,296,809 discloses that up to 20 slides are mounted in a circular array to a carousel (See column 3, lines 44-45). Each slide receives reagents, e.g. DNA probe (See column 3, lines 48-50, and column 6, lines 15-19). Glass slides rest against plate (See column 10, lines 21-23). Therefore based upon the teachings of US 6,296,809, Towne et al. US 6,855,552 is qualified as a prior art.

5. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schwartz (4,886,741, issued December 12, 1989) as applied to claims 9-14 and 19-21 above, and further in view of Richards et al. (6,296,809, issued Oct. 2, 2001).

Richards et al. disclose apparatus and methods for automatically staining or treating multiple tissue sample mounted on glass slides (See column 3, lines 29-30). Richards et al. disclose that up to 20 slides are mounted in a circular array to a carousel (See column 3, lines 44-45). Each slide receives reagents, e.g. DNA probe (See column 3, lines 48-50, and column 6, lines 15-19). Glass slides rest against plate (See column 10, lines 21-23).

One of ordinary skill in the art would have been motivated to apply a probe composition which is arrayed on a solid substrate as taught by Richards et al. because as taught by Richards et al. each sample can receive an individualized staining or treatment protocol even when the protocol requires different temperature and thus different DNA probes will be running simultaneously (See column 3, lines 31-34). It would have been prima facie obvious to apply a probe composition arrayed on a solid substrate.

Summary

6. No claims are allowable.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (571) 272-0790. The examiner can normally be reached on Monday - Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Joyce Tung
January 23, 2008

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
2/4/08